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PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference P1204-JA	**FOR FURTHER ACTION**	See Form PCT/IPEA/416
International application No. PCT/EP2004/007195	International filing date *(day/month/year)* 30.06.2004	Priority date *(day/month/year)* 30.06.2003

International Patent Classification (IPC) or national classification and IPC
G01N33/574, C12Q1/68, A61P35/00

Applicant
PROGENIKA BIOPHARMA, S.A.

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 7 sheets, including this cover sheet.
3. This report is also accompanied by ANNEXES, comprising:
   a. ☐ *sent to the applicant and to the International Bureau)* a total of sheets, as follows:
      ☐ sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).
      ☐ sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.
   b. ☐ *(sent to the International Bureau only)* a total of (indicate type and number of electronic carrier(s)) , containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).

4. This report contains indications relating to the following items:

☒	Box No. I	Basis of the opinion
☐	Box No. II	Priority
☐	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
☐	Box No. IV	Lack of unity of invention
☒	Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
☐	Box No. VI	Certain documents cited
☐	Box No. VII	Certain defects in the international application
☐	Box No. VIII	Certain observations on the international application

Date of submission of the demand	Date of completion of this report
29.04.2005	27.06.2005
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized Officer Hoesel, H Telephone No. +49 89 2399-8693

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/EP2004/007195

Box No. I Basis of the report

1. With regard to the **language**, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.

   ☐ This report is based on translations from the original language into the following language , which is the language of a translation furnished for the purposes of:

   ☐ international search (under Rules 12.3 and 23.1(b))
   ☐ publication of the international application (under Rule 12.4)
   ☐ international preliminary examination (under Rules 55.2 and/or 55.3)

2. With regard to the **elements*** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

Description, Pages

1-25 as originally filed

Sequence listings part of the description, Pages

1-6 as originally filed

Claims, Numbers

1-36 received on 06.05.2005 with letter of 29.04.2005

Drawings, Sheets

1/2, 2/2 as originally filed

☒ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing

3. ☐ The amendments have resulted in the cancellation of:

   ☐ the description, pages
   ☐ the claims, Nos.
   ☐ the drawings, sheets/figs
   ☐ the sequence listing *(specify)*:
   ☐ any table(s) related to sequence listing *(specify)*:

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

   ☐ the description, pages
   ☐ the claims, Nos.
   ☐ the drawings, sheets/figs
   ☐ the sequence listing *(specify)*:
   ☐ any table(s) related to sequence listing *(specify)*:

* *If item 4 applies, some or all of these sheets may be marked "superseded."*

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/EP2004/007195

Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-18,21,23,28,29,31-36
	No:	Claims	19,20,22,24-27,30
Inventive step (IS)	Yes:	Claims	1-18,21,23,28,29,32,35,36
	No:	Claims	19,20,22,24-27,30,31,33,34
Industrial applicability (IA)	Yes:	Claims	1-36
	No:	Claims	

2. Citations and explanations (Rule 70.7):

see separate sheet

Supplemental Box relating to Sequence Listing

Continuation of Box I, item 2:

1. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this report has been established on the basis of:

   a. type of material:

   ☒ a sequence listing

   ☐ table(s) related to the sequence listing

   b. format of material:

   ☒ in written format

   ☒ in computer readable form

   c. time of filing/furnishing:

   ☒ contained in the international application as filed

   ☒ filed together with the international application in computer readable form

   ☐ furnished subsequently to this Authority for the purposes of search and/or examination

   ☐ received by this Authority as an amendment on

2. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table(s) relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

3. Additional observations, if necessary:

Reference is made to the following documents:

D1: WO 03/031930 A, 17 April 2003
D2: WO 01/14420 A, 1 March 2001
D3: WO 2004/050914 A, 17 June 2004
D4: CIRCOSTA PAOLA ET AL, BLOOD, vol. 98/11 Part 1, 16 November 2001, page 360a, XP009041247 & 43RD ANNUAL MEETING OF THE AMERICAN SOCIETY OF HEMATOLOGY, PART 1; ORLANDO, FLORIDA, USA; DECEMBER 07-11, 2001 ISSN: 0006-4971
D5: GIESEG MICHAEL A ET AL, BMC BIOINFORMATICS [ELECTRONIC RESOURCE]. 30 SEP 2002, vol. 3, no. 1, 30 September 2002 (2002-09-30), page 26, XP002309629 ISSN: 1471-2105

SECTION V:

1. The prior art is silent as to correlation of plexin B1 expression which is diagnostically significant for renal cancer. The prior art taken in to consideration also fails to provide evidence or suggestions as to its active participation in the development of renal cancer.

   Consequently the method as defined in claims 1 - 18 is considered as novel and inventive within the meaning of Art. 33(2) and (3) PCT.

   The same applies to the medical and technical uses as defined in claims 21, 23, 32, 35 and 36.

2. Claim 19 and claim 20 in its present wording relate to a product, i.e. to a recombinant expression vector coding for Plexin B1 protein.

   Recombinant expression of this protein and the accordingly designed vectors were known and applied prior to the effective date of this application see, for instance, D2, examples 1 - 3 and 8, Seq Id No 10, or D4, the abstract).

The products of claims 19 and 20, thus lack novelty.

The objection similarly applies to claim 22, which claim is according to the PCT interpreted as a true product claim.

3. Claims 24 and 25 relate to the second medical use of a compound that is defined in terms of its desired activity only. This functional definition does not allow to deduce any structural motifs required for the desired activity and thus is not suitable as limitation with respect to toxins and chemotherapeutic agents and combination medicaments, conventionally used in the treatment of renal cancer.

Thus, claims 24 and 25 are not acceptable for lack of clarity (Art. 6 PCT) and lack of limitation (Art. 33(2) PCT).

The said objections analogously apply to the compositions as defined in claims 26, 27 (particular having regard to option (b)) and 30.

4. With respect to medical utility of plexin B1, D1 is the closest state of the art. The evidence presented for clinical utility consists of observation of a cancer-related overexpression of the marker and thus would, at best, suggest therapeutic use of plexin B1 antagonists or plexin B1 binding agents.

A composition as defined in claims 28 and 29 is thus considered as novel and inventive in view of the prior art taken into consideration (Art. 33(2) and (3) PCT).

5. D2 and D4 disclose amplification of plexin B1 by way of RT-PCR. D1, additionally, discloses a diagnostic utility of a plexin B1 tests. As the provision of kits for assay of clinical interest is commonplace, the subject-matter of claim 31, 33 and 34 is considered to lack inventive step (Art. 33(3) PCT).

The intended use does not discriminate the given products from products taught or suggested by the prior art.

6. D3 claims the priority date of 29.11.2002. It identifies wt plexin B1 as tumour suppressor (p. 55, lines 29 - 32) and cancer-associated plexin B1 mutations. It particularly discloses amplification of Plexin B1 nucleic acids (mutant and wildtype form) and kits comprising corresponding primer pairs (p. 7, lines 5 - 12, p. 12, lines 6 - 11, p.16 line 28 - p. 17, line 1), as well as antisense RNA, antibodies specific for wt- or mutant plexin B1 and wt plexin B1 nucleic acid as potential therapeutical agents (p. 33, lines 13 - 28, p. 35, line 27 - p. 36, line 31, p. 43, line 29 - p. 44, line 19).

Its content might be taken into consideration during the regional phase, particularly with respect to the subject-matter of claims 19, 20, 22, 26 - 29, 31, 33 and 34.